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# Sex differences in the relation between prenatal maternal emotional complaints and child outcome

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#### ABSTRACT

*Background:* Sex differences are found in animal studies concerning the relationship between prenatal maternal stress and outcome of the offspring. Most human studies in this field have not addressed sex differences, although differences between boys and girls may elucidate the biochemical as well as psychological processes involved. Associations between prenatal maternal emotional complaints and behavioural problems of toddlers and preschoolers as assessed by both mothers and fathers are studied separately for boys and girls.

*Methods:* Healthy Dutch Caucasian singleton, pregnant women (N = 444) answered questionnaires about anxiety and depression in every trimester of pregnancy. When their children (227 boys, 217 girls) were between 14 and 54 months old, both parents reported on their current feelings of depression and anxiety and on the behavioural problems of their children.

*Results:* Prenatal maternal emotional complaints were found to be associated with child behavioural problems both in boys and in girls, but in different ways. Prenatal maternal emotional complaints during the first trimester were associated with total and internalizing behavioural problems for boys. Emotional complaints during the third trimester were associated with total, internalizing, as well as externalizing behavioural problems for girls. *Conclusions:* Differentiation according to sex and information on timing of emotional complaints during pregnancy is needed in studies concerning the relation between prenatal maternal emotional complaints and child outcome.

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#### 1. Introduction

Children of women with complaints reflecting distress, anxiety or depression during pregnancy, show more difficulties in motor, cognitive, and especially socio-emotional development from infancy to adolescence [1,2]. Several mechanisms have been proposed to explain these relations. First, the function of the hypothalamic-pituitary-adrenal (HPA) system may have been affected by prenatal maternal distress [1]. In addition, genetic factors or sex hormones may also be important in the processes that affect the developing fetus as a result from maternal distress [3,4]. The Developmental Origins of Health and Disease (DOHaD) approach states that the fetus will adapt and develop by shaping and structuring the organs for optimal performance in the fetal environment and maternal distress may elicit such biological programming processes [5].

Animal studies have shown different effects of prenatal stress on postnatal outcomes for male and female offsprings. Several animal studies indicated an effect of prenatal stress on the hypothalamic-

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pituitary-adrenal (HPA) function, specifically for females and showed more prominent, mainly externalizing behaviour of the female offspring [6,7]. Only a few studies have addressed sex differences in humans. Van den Bergh et al. [8] reported that antenatal exposure to maternal anxiety at 12-22 weeks pregnancy was associated with a high and more flattened cortisol dav-time profile in both sexes and, in female adolescents only, with depressive symptoms. Rodriguez and Bohlin [9] found a significant association between prenatal stress experienced around the 10th week of pregnancy and ADHD symptoms in boys only. Martin et al. [10] found a stronger correlation for 5-year-old boys between maternal distress during the first trimester of pregnancy and ratings of negative emotionality. O'Connor et al. [11] however, found that high levels of anxiety at 32 weeks gestation were associated significantly with hyperactivity and inattention in 4-year-old boys, and with behavioural and emotional problems in boys as well as girls. They also found that high levels of anxiety at 18 weeks gestation were associated with more behavioural and emotional problems in girls at 81 months [12]. Hence, the available results are inconsistent for the nature of sex differences, the timing of distress during pregnancy and the nature of the maternal complaints involved. In this study, the association between prenatal maternal depressive and anxious complaints during different trimesters in pregnancy and externalizing and internalizing behavioural problems of the children is studied separately for boys and girls at toddler or preschool age, with both mothers and fathers as informants.

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#### 2. Methods

#### 2.1. Participants

Between July 2002 and May 2005, midwives working in seven community midwifery practices in the southern regions of the Netherlands, invited healthy Dutch Caucasian singleton pregnant women (complete information was available for 1093 women) to participate in the study at their first antenatal check-up, at 10-12 weeks' gestation [13]. After pregnancy, the women were asked to give informed consent to participate in future follow-up studies. In total 444 (response rate of 41%) mothers agreed to participate in the follow-up study and returned questionnaires about their current emotional complaints and behavioural problems of their children. The participating mothers did not differ from the non-participants in prenatal emotional complaints, maternal age at birth and marital status. However, the mothers who participated did have a higher educational level than non-participants (5.3% vs 10.2% for low education; 55.2% vs 54.9% for middle education; 39.5% vs 34.8% for higher education, p < .01). Participating mothers smoked less during pregnancy than non-participating mothers. Furthermore, the children of mothers who participated had a 107 g higher mean birth weight and 0.45 week longer mean gestation duration compared to the children of non-participating mothers.

At delivery, the 444 participating women ranged in age from 19 to 42 years (M = 30.7, SD = 3.7) and 98% were married or living together with the father of their children. Their partners ranged in age from 23 to 47 years (M = 33.0, SD = 3.9). Half of the women were primiparous (N=219, 50.3%). 5.9% of the women finished primary education, 51.2% attended secondary education and 42.9% completed higher education or university. Almost 10% (9.6%) of their partners completed primary education, 45.6% attended secondary education and 44.9% finished higher education or university. The majority of the women (87.3%) did not smoke during pregnancy, 11.5% smoked less then 10 cigarettes a day and 1.2% smoked more than 10 cigarettes a day. Alcohol intake during pregnancy was rare. The infants (227 boys, 51.1%; 217 girls, 48.9%) were assessed between the ages of 14-54 months (age range boys 14-53 months, M = 29.4, SD = 10.3; age range girls 15–54 months, M = 29.8, SD = 10.6). All of the infants were born at term with a mean gestational age of 39.8 weeks (SD = 1.3 weeks) and a mean birth weight of 3527 g (SD = 479 g). 110 women (24.8%) gave birth to another baby after the target child was born.

#### 2.2. Measures

#### 2.2.1. Depression

Prenatal depression of the mothers was assessed using the Dutch version of the Edinburgh Depression Scale (EDS; [14,15]). The EDS is a widely used 10-item self-report scale designed as a screening instrument for depression and has been shown valid in and outside the postnatal period. Items are scored on four-point rating scales. Total scores range between 0 and 30, with a cut-off score of 12 and higher [16] to indicate mild to severe depressive symptoms (mean 5.89, SD = 4.03) [15]. Current depressive complaints of both parents were also assessed with the EDS.

#### 2.2.2. Anxiety

Prenatal anxiety of the mothers was assessed with the state version of the State-Trait Anxiety Inventory (STAI; [17]). The STAI consists of two subscales each containing 20 items. The state anxiety subscale measures transient anxiety or anxiety at the moment of scoring. Trait anxiety measures dispositional anxiety or anxiety in general. The State version was used to assess the feelings of anxiety of the women during a specific period in their pregnancy. Total scores on the State subscale ranges between 20 and 80. The Dutch version of the STAI has been validated previously (normal population mean for women <40 years = 38.0, SD = 12.8) [18].

Prenatal as well as current anxiety was assessed with the anxiety scale of the Symptom Check List (SCL-90; [19]). The SCL-90 has been validated before in the Netherlands and its use as well as the use of several subscales only, has revealed appropriate psychometric properties [20]. Total scores of the anxiety scale ranges between 10 and 50 (normal population mean for women = 13.43, SD = 4.91; for men: 12.23, SD = 3.80) [20].

#### 2.2.3. Child assessment

When the children were between 14 and 54 months old, both parents completed the Child Behaviour Check List (CBCL 11/2–5) to evaluate the behaviour of their children [21]. The CBCL 11/2–5 is a parent-completed questionnaire that contains 100 behavioural and emotional problem items, for which is indicated if a problem is seen sometimes (1), frequently (2) or not (0). Next to a total scale score, the results are differentiated according to *internalizing* (anxiety, depression, withdrawn behavior) or *externalizing* (attention difficulties, aggressive behaviour) problems. Raw scores are converted, based on the age and gender of the child, into standardized *T* scores. The standardized *T* scores can be compared for boys and girls from 11/2 to 5 years. A norm referenced *T*-score of >70 is considered to be in the clinical range. Norm referenced *T*-scores of 65–70 are considered to be in the borderline-clinical range [21].

#### 2.3. Procedures

Most studies concerning prenatal maternal emotional complaints and developmental outcome of the children use data based on maternal (self-) reports. However it is most likely that emotional complaints of mothers continue or recur after birth and possibly affect the mothers' ratings or perceptions of their children's behaviour. This may result in a reporter bias, as anxious or depressed mothers might be more likely to misinterpret disturbances in their children [11,22]. It is also found that 80% of depressive symptoms are recurrent [23]. Therefore, to obtain information from multiple informants, also fathers' report of the behaviour of their daughters and sons were included.

When the children were between 1 and 5 years of age both parents were also asked to answer questionnaires about their own current emotional complaints. Current sociodemographic information was obtained through a background questionnaire for both parents. Maternal emotional complaints (depression and anxiety) had been assessed at

#### Table 1

Descriptive information for maternal prenatal EDS, STAI, and SCL scores and both parents' scores on EDS and SCL at time of child assessment (current emotional complaints) (*N* between 194 and 227).

	EDS		STAI		SCL	
	Boys	Girls	Boys	Girls	Boys	Girls
12 wk GA:						
M (SD)	5.0 (4.01)	4.7 (3.93)	29.6 (8.05)	29.4 (8.24)	12.2 (2.78)	12.3 (3.77)
Range	0–18	0–22	20-60	20-63	10-22	10–38
24 wk GA:						
M (SD)	4.5 (4.21)	3.8 (3.93)	30.0 (8.61)	29.3 (8.41)	12.5 (3.20)	12.0 (3.11)
Range	0–25	0–17	20-61	20-64	10-33	10–29
36 wk GA:						
M (SD)	4.8 (4.18)	3.7 (3.75)*	31.9 (9.48)	31.4 (9.23)	12.9 (3.55)	12.5 (3.39)
Range	0–21	0–17	20-69	20-64	10-30	10–30
Current maternal scores						
M (SD)	4.6 (4.32)	4.6 (4.58)			11.9 (3.71)	12.0 (4.97)
Range	0–22	0–20			10-34	10–39
Current paternal scores						
M (SD)	2.9 (3.07)	3.3 (3.48)			11.1 (3.05)	11.2 (3.64)
Range	0-13	0-18			10-34	10-45

wk GA: weeks gestation, EDS: Edinburgh Depression Scale, STAI: State Trait Anxiety Inventory.

SCL: Symptom Check List.

\*p < .05 (difference between boys and girls on EDS at 36 wk GA).

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